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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/683,815	10/09/2003	Arnon Rosenthal	PC19490A	5142
23913	7590	10/24/2007		
PFIZER INC Steve T. Zelson 150 EAST 42ND STREET 5TH FLOOR - STOP 49 NEW YORK, NY 10017-5612			EXAMINER BALLARD, KIMBERLY A	
			ART UNIT 1649	PAPER NUMBER
			MAIL DATE 10/24/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/683,815	Applicant(s) ROSENTHAL ET AL.	
	Examiner Kimberly A. Ballard	Art Unit 1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 August 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-14,16-27,29-38 and 51-53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-14,16-27,29-38 and 51-53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) ☐ Notice of References Cited (PTO-892) | 4) ☐ Interview Summary (PTO-413) |
| 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) ☐ Information Disclosure Statement(s) (PTO/SB/08) | 5) ☐ Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) ☐ Other: _____ |

DETAILED ACTION

Response to Amendment

1. Claims 1, 2, 8, 9, 13, 14, 20, 21, 26, 27, 33 and 34 have been amended as requested in the response filed August 7, 2007. Following the amendment, claims **1, 2, 4-14, 16-27, 29-38, and 51-53** are pending and under examination in the instant office action.

Withdrawn Objections and Claim Rejections

2. The objection to claims 8, 9, 20, 21, 33 and 24, as set forth at ¶ 11 of the previous Office action (mailed 02/07/2007), is withdrawn in view of Applicants' amendments to the claims.

3. The rejection of claims 1, 2, 4-14, 16-27, 29-38 and 51-53 under 35 U.S.C. 112, 2nd paragraph, as set forth at ¶ 16 of the previous Office action (02/07/2007) is withdrawn in view of Applicants' amendments to the claims.

4. Applicants' arguments, see pages 8-11 of the response filed August 7, 2007, and in particular page 8, with respect to claims 1-12 and 51 have been fully considered and are persuasive. The rejection of claims 1-12 and 51 under 35 U.S.C. 112, first paragraph, has been withdrawn.

Maintained Claim Rejections

Obviousness-Type Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. The provisional rejection of instant claims 1, 2, 4, 6, 10-14, 16, 18, 22-24, 26, 27, 29, 31, 35-37 and 51-53 over claims 1, 2, 4, 7-17, 19, 28, 30-40 and 42 of copending Application No. 11/194,989 is maintained for reasons of record set forth in the office action dated 01/31/2006 and held in abeyance until all other rejections are resolved.

7. The provisional rejection of instant claims 1, 2, 4, 6, 10-14, 16, 18, 22-24, 26, 27, 29, 31, 35-37 and 51-53 over claims 1-3, 6-15, 17, 26, 28-38 and 40 of copending

Application No. 11/195,207 is maintained for reasons of record set forth in the office action dated 01/31/2006 and held in abeyance until all other rejections are resolved.

8. The provisional rejection of instant claims 1, 2, 10, 13, 14, 22, 26, 27 and 35 over claims 41-43 of copending Application No. 11/413,817 is maintained for reasons of record set forth in the office action dated 02/07/2007 and held in abeyance until all other rejections are resolved.

Claim Rejections – 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. The rejection of claims 1, 2, 4-14, 16-27, 29-38 and 51-53 under 35 U.S.C. 102(e) as being anticipated by US 2003/0073655 A1 by Chain (published 04/17/2003, filed 02/28/2002), as evidenced by Zeitlin et al. (*Microbes Infection*, 2000; 2: 701-708) is maintained for reasons of record.

In the response filed August 7, 2007, Applicants assert that the disclosure by Chain does not teach or suggest each and every element of the present claims. In particular, Applicants argue that even using the principle of inherency, Chain does not

anticipate claims 4-7, 16-19 and 29-32, regarding antibody binding affinities. Applicants thus submit that "the binding limitations have not been met by Chain", and relying on the secondary reference (Zeitlin) for establishing "typical" monoclonal binding affinities does not remedy the situation. Accordingly, Applicants argue "even if the recited binding limitations had in fact been met by Chain, no explanation as to why competitive inhibition of the binding of other monoclonal antibodies would be an "expected" property of the Chain antibodies is provided."

Applicant's arguments filed August 7, 2007 have been fully considered but they are not persuasive. With respect to Applicants' argument that binding affinity limitations of the prior art antibodies have not been met, Applicants are directed to MPEP § 2112, section V, which states:

Once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the Examiner presents evidence or reasoning tending to show inherency, the burden shifts to the Applicant to show an unobvious difference.

In the instant case, evidence has been presented to demonstrate what the skilled artisan would reasonably expect as a binding affinity for an antibody, particularly a monoclonal antibody. Zeitlin et al. clearly indicate that expected antibody-binding affinities for monoclonal antibodies (i.e., in the range of 10^{-8} to 10^{-10} M) would encompass the instantly claimed antibodies of claims 4-7, 16-19 and 29-32. It is thus Applicants' burden to show unobvious difference as the PTO has insufficient resources to compare the teachings of the prior art reference and that of Applicants' claims.

With respect to Applicants' assertions that "even if the recited binding limitations had in fact been met by Chain, no explanation as to why competitive inhibition of the binding of other monoclonal antibodies would be an "expected" property of the Chain antibodies is provided," it is first noted that the claims reciting epitope/competitive inhibition limitations, such as claims 8, 9, 20, 21, 33 and 34, are not dependent from any claims reciting antibody binding affinity. Regardless, as discussed in the previous Office action, Chain discloses free end specific antibodies targeted to amino acids 33-40 (or 34-40 or 36-40 or 37-40) of C-terminus-truncated A β -peptides in addition to free carboxylic (COOH) groups (see [0076]). The monoclonal antibody (mAb) comprising the amino acid sequences of SEQ ID NOs: 4 and 6, which is disclosed as mAb 2286 in the instant specification, is noted to bind to an epitope which includes at least residues 39 and/or 40 of the A β ₁₋₄₀ peptide and comprises at least residues 36-40 of A β ₁₋₄₀ (see [0184] and [0187] of the instant application). Thus, Chain's antibodies, which are directed to epitopes of amino acid residues 33-40, 34-40, 36-40 or 37-40 of the A β ₁₋₄₀ peptide, would bind to the same epitope as the instantly claimed antibody, and therefore would be expected to competitively inhibit binding of the presently claimed 2286 monoclonal antibody. Accordingly, the teachings of Chain clearly anticipate the instantly claimed invention, and the rejection of claims 1, 2, 4-14, 16-27, 29-38 and 51-53 is maintained.

11. The rejection of claims 1, 2, 4-14, 16-27, 29-38 and 51-53 under 35 U.S.C. 102(e) as being anticipated by US 2004/0241164 A1 by Bales et al., published

December 2, 2004, filed August 14, 2002 (on Applicant's IDS) is maintained for reasons of record.

In the response filed August 7, 2007, Applicants argue that the disclosure of Bales does not teach or suggest each and every element of the present claims. In particular, Applicants note that Bales teaches the antibody 266, which recognizes epitopes between amino acids 13 and 28 of A β , not between amino acids 28 and 40 as presently claimed. Applicants also assert that Bales neither teaches nor suggests a preference for antibodies without cross-reactivity to A β_{1-42} and A β_{1-43} peptides, and further note that most of the antibodies disclosed by Bales are shown to bind to A β_{1-42} . Additionally, Applicants argue that nowhere does Bales teach or suggest the properties of the disclosed 2G3 antibody as binding to an epitope that includes amino acids 39 and/or 40 of the A β_{1-40} peptide, or to competitively inhibit the presently claimed monoclonal antibody. Moreover, Applicants assert that Bales does not provide an enabling disclosure of the 2G3 antibody, wherein "no evidence is provided that 2G3 would be effective for the treatment of Alzheimer's disease or any symptoms thereof, even in mice, let alone in humans."

Applicant's arguments filed August 7, 2007 have been fully considered but they are not persuasive. While the Bales reference does disclose the 266 antibody, this antibody is not relied upon for anticipation of the present claims. It is Bales' disclosure in general directed to therapeutic treatment of Alzheimer's disease comprising administration of high affinity A β antibodies, and the 2G3 antibody in particular that form the basis of the anticipatory reference teachings. It is noted that MPEP § 2123 states:

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"The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting *In re Lemelson*, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)).

A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill in the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See also *Upsher-Smith Labs. v. Pamlab, LLC*, 412 F.3d 1319, 1323, 75 USPQ2d 1213, 1215 (Fed. Cir. 2005) (reference disclosing optional inclusion of a particular component teaches compositions that both do and do not contain that component); *Celeritas Technologies Ltd. v. Rockwell International Corp.*, 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir. 1998) (The court held that the prior art anticipated the claims even though it taught away from the claimed invention. "The fact that a modem with a single carrier data signal is shown to be less than optimal does not vitiate the fact that it is disclosed.").

Therefore, while the 266 antibody disclosed by Bales may be a preferred embodiment, the 2G3 antibody is still prior art and anticipatory for all that it teaches. Bales discloses that the 2G3 antibody recognizes A β 40 but not A β 42. Based on this statement, the skilled artisan would understand that the antibody must recognize a C-terminal epitope of the A β protein, such as an epitope comprising residues 39 and/or 40 of A β , in order for

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the antibody to distinguish between the A β 40 and A β 42 peptides. The instantly claimed 2286 antibody is disclosed as having an epitope that comprises *at least* residues 36-40 of A β ₁₋₄₀ (see [0184] and [0187] of the instant application). The skilled artisan would know that an antibody's epitope spans several residues. Therefore, the 2G3 antibody would reasonably be expected to recognize an epitope comprising residues 39 and/or 40 of A β , the antibody would also be reasonably expected to competitively inhibit binding of the 2286 antibody to the A β 1-40 peptide as well as bind to the same epitope as the 2286 antibody.

With regard to Applicants' argument that the Bales reference is non-enabling, MPEP § 2121 notes that:

When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable.

Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). See also MPEP § 716.07.

Thus, it is Applicants' burden to show unobvious difference as the PTO has insufficient resources to compare the teachings of the prior art reference and that of Applicants' claims. Reasons showing inherency have clearly been shown, both here and of record, and there are no structural limitations to the claimed antibodies, their amounts or administration that teach over the prior art reference. There is no precedent in the cited case law to conclude that Bales is non-enabled. As noted previously, the above appears to be more a question of fact to which Applicants have shown no evidence or

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scientific reasoning that would disprove the teachings of Bales, and thus Applicants' questioning of Bales' enablement reflects upon the enablement of the instant claims, as the Bales teachings are not differentiated therefrom. Accordingly, the teachings of Bales et al. fully anticipate the present invention and thus the rejection of claims 1, 2, 4-14, 16-27, 29-38 and 51-53 is maintained.

Conclusion

12. No claims are allowed.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Ballard whose telephone number is 571-272-4479. The examiner can normally be reached on Monday-Friday 9AM - 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kimberly Ballard, Ph.D.
October 17, 2007

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646